

69/418,221

for reducing cerebral infarct vol.

L4 ANSWER 3 OF 3 CA COPYRIGHT 2000 ACS

ACCESSION NUMBER: 129:90287 CA

TITLE: Sonic hedgehog protein: a novel approach to the treatment of neurodegenerative disorders?

AUTHOR(S): Pang, Kevin; Ingolia, Thomas D.

CORPORATE SOURCE: Ontogeny Inc., Cambridge, MA, USA

SOURCE: CNS Drugs (1998), 9(4), 253-259

CODEN: CNDREF; ISSN: 1172-7047

PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Sonic hedgehog is a member of a newly discovered family of mols. that are active during development in vertebrates. Sonic hedgehog induces development of key CNS neuronal cell types, including the dopaminergic neurons that are destroyed in Parkinson's disease. In addn. to developmental-inducing activity, Sonic hedgehog has neurotrophic and neuroprotective activities on many of these same cell types. These activities suggest interesting clin. potentials for Sonic hedgehog in neurodegenerative diseases such as Parkinson's disease and in acute CNS trauma such as stroke.

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(FILE 'HOME' ENTERED AT 15:59:51 ON 18 NOV 2000)

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L1 0 S PTC(10W)THERPEUTIC#

L2 309 S PTC(10W)THER?

L3 1 S L2 AND STROKE

L4 3 S NEUROPROTEC?(10W)HEDGEHOG(10W)PROTEIN#

=> s 12 not 13

L5 308 L2 NOT L3

=> s 15 and ptc

2309 PTC

L6 308 L5 AND PTC

=> s 16 and patched binding peptide

536 PATCHED

612303 BINDING

236178 PEPTIDE

0 PATCHED BINDING PEPTIDE

(PATCHED(W)BINDING(W)PEPTIDE)

L7 0 L6 AND PATCHED BINDING PEPTIDE

=> s 16 and neuron?

133007 NEURON?

L8 2 L6 AND NEURON?

=> d 18 1-2 ibib ab

L8 ANSWER 1 OF 2 CA COPYRIGHT 2000 ACS
 ACCESSION NUMBER: 133:41366 CA
 TITLE: The normal patched allele is expressed in
 medulloblastomas from mice with heterozygous
 germ-line
 mutation of patched
 AUTHOR(S): Wetmore, Cynthia; Eberhart, Derek E.; Curran, Tom
 CORPORATE SOURCE: Departments of Developmental Neurobiology and
 Hematology/Oncology, St. Jude Children's Research
 Hospital, Memphis, TN, 38105, USA
 SOURCE: Cancer Res. (2000), 60(8), 2239-2246
 CODEN: CNREA8; ISSN: 0008-5472
 PUBLISHER: American Association for Cancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Defects in a developmental signaling pathway involving mammalian homologs
 of the Drosophila segment polarity gene, patched (**ptc**) and its
 ligand, sonic hedgehog (shh), contribute to tumor formation in several
 tissues. Recently, a subset of medulloblastoma, the most common
 malignant
 brain tumor in children, was found to contain somatic mutations in the
 human **ptc** gene. In addn., basal cell nevus syndrome (BCNS), or
 Gorlin syndrome, which is characterized by developmental anomalies and a
 predisposition to skin and nervous system malignancies, is assocd. with
 germ-line mutation of **ptc**. Targeted disruption of both alleles
 of **ptc** in mice results in embryonic lethality. However,
ptc^{+/-} mice survive and develop spontaneous cerebellar brain
 tumors, suggesting that **ptc** may function as a tumor suppressor
 gene. Therefore, we investigated **ptc**^{+/-} mice as a model for
 human medulloblastoma. We report that 14% of **ptc**^{+/-} mice
 develop central nervous system tumors in the posterior fossa by 10 mo of
 age, with peak tumor incidence occurring between 16 and 24 wk of age.
 The
 tumors exhibited several characteristics of human medulloblastoma,
 including expression of intermediate filament proteins specific for
 neurons and glia. Full-length **ptc** mRNA was present in
 all tumors analyzed, indicating that there was no loss of
 heterozygosity at the **ptc** locus. Nucleotide sequence of
ptc mRNA from four tumors failed to identify any mutations.
 However, a comparison of the normal **ptc** sequence from C57BL/6
 and 129Sv mice did reveal several polymorphisms. High levels of glil
 mRNA
 and protein were detected in the tumors, suggesting that the shh/
ptc pathway was activated despite the persistence of **ptc**
 expression. These data indicate that haploinsufficiency of **ptc**
 is sufficient to promote oncogenesis in the central nervous system.
 REFERENCE COUNT: 49
 REFERENCE(S): (1) Aszterbaum, M; J Investig Dermatol 1998, V110,
 P885 CA
 (3) Capdevila, J; EMBO J 1994, V13, P71 CA
 (4) Chen, Y; Cell 1996, V87, P553 CA
 (7) Dahmane, N; Development (Camb) 1999, V126, P3089
 CA
 (8) Dahmane, N; Nature (Lond) 1997, V389, P876 CA
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 2 CA COPYRIGHT 2000 ACS
 ACCESSION NUMBER: 130:205165 CA
 TITLE: Regulation of muscle tissue formation and/or
 maintenance with hedgehog proteins and **ptc**
therapeutics and treatment or prevention of
 muscular disorders
 INVENTOR(S): Bladgen, Chris S.; Currie, Peter D.; Ingham, Philip

W.; Hughes, Simon M.
 PATENT ASSIGNEE(S): Ontogeny, Inc., USA
 SOURCE: PCT Int. Appl., 130 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9910004	A2	19990304	WO 1998-US17922	19980828
WO 9910004	A3	19990527		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9891252	A1	19990316	AU 1998-91252	19980828
EP 1009424	A2	20000621	EP 1998-943462	19980828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1997-57394	19970829
			WO 1998-US17922	19980828

OTHER SOURCE(S): MARPAT 130:205165

AB The present application relates to a method for modulating the formation and/or maintenance of muscle tissue by ectopically contacting muscle cells, esp. muscle stem/progenitor cells, in vitro or in vivo, with a hedgehog therapeutic or **ptc therapeutic** in an amt. effective to alter the growth state of the treated cells. The hedgehog therapeutic comprises a hedgehog protein modified with one or more lipophilic moieties, e.g., sterols, fatty acids, or arom. hydrocarbons. The **ptc therapeutics** mimic hedgehog-mediated patched signal transduction by binding to patched or altering localization, protein-protein binding and/or enzymic activity of intracellular proteins involved in patched signal transduction. Such therapeutics included antisense oligonucleotides and protein kinase A inhibitors. Expts. in zebrafish suggested that SHH may initiate slow myoblast formation but that continued exposure is not required to trigger terminal differentiation of slow muscle fibers.

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 L7 0 S L6 AND PATCHED BINDING PEPTIDE
 L8 2 S L6 AND NEURON?

=> log y

COST IN U.S. DOLLARS

SINCE FILE
ENTRY

TOTAL
SESSION

FULL ESTIMATED COST

31.87

32.02

DISCOUNT AMOUNTS (F QUALIFYING ACCOUNTS)

SIN FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-2.65

-2.65

STN INTERNATIONAL LOGOFF AT 16:05:52 ON 18 NOV 2000